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	<p><input type="checkbox"/> 1 Lorentsen RH, Fynbo CH, Thøgersen HC, Etzerodt M, Holtet TL.</p> <p> Targeting and amplification of immune killing of tumor cells by pro-Smac. Int J Cancer. 2004 Mar;109(1):85-94. PMID: 14735472 [PubMed - indexed for MEDLINE]</p> <p><input type="checkbox"/> 2 Li R, Rüttinger D, Urba W, Fox BA, Hu HM.</p> <p> Targeted delivery of human pro-apoptotic enzymes to tumor cells: In vitro studies describing a novel class of recombinant highly cytotoxic agents. Mol Cancer Ther. 2003 Dec;2(12):1341-50. PMID: 14707275 [PubMed - indexed for MEDLINE]</p> <p><input type="checkbox"/> 3 Liu Y, Cheung LH, Hittelman WN, Rosenblum MG.</p>	<p>Related Articles, Links</p> <p>Related Articles, Links</p> <p>Related Articles, Links</p>

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L2	89	(site or motif or sequence or target) near4 (granzyme b)	US-PGPUB; USPAT	ADJ	OFF	2007/12/18 20:13
L3	80	(granzyme b) near4 (cleavage or cleave or cleaved)	US-PGPUB; USPAT	ADJ	OFF	2007/12/18 20:13
L4	4412	I1 near8 (fusion protein)	US-PGPUB; USPAT	ADJ	OFF	2007/12/18 20:14
L5	2	I1 and I2 and I3 and I4	US-PGPUB; USPAT	ADJ	OFF	2007/12/18 20:14

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L3 296 (GRANZYME B) (4A) (CLEAVAGE OR CLEAVE OR CLEAVED OR CLEAVING OR

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DUPLICATE 1

AN 2004034626 MEDLINE

DN PubMed ID: 14735472

TI Targeting and amplification of immune killing of tumor cells by pro-Smac.

AU Li Rui; Ruttinger Dominik; Urba Walter; Fox Bernard A; Hu Hong-Ming

CS Laboratory of Cancer Immunobiology, Earle A Chiles Research Institute,

Providence Portland Medical Center, Portland, OR 97213, USA.

NC R01 CA92254 (NCI)

SO International journal of cancer. Journal international du cancer, (2004

Mar) Vol. 109, No. 1, pp. 85-94.

Journal code: 0042124. ISSN: 0020-7136.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LA English

FS Priority Journals

EM 200403

ED Entered STN: 22 Jan 2004
Last Updated on STN: 13 Mar 2004
Entered Medline: 12 Mar 2004

AB Overexpression of inhibitors of apoptosis (IAP) is one potential mechanism for tumor cells to evade immune surveillance. To determine whether immune-mediated killing of tumor cells can be enhanced by neutralization of IAP proteins, 2 novel eGFP-Smac fusion proteins (pro-Smac) were introduced into the poorly immunogenic mouse melanoma cell line, B16BL6-D5 (D5). Each fusion protein contained Smac and a cleavage site specific for granzyme B (GrB) or caspase 8, thereby targeting the 2 major killing mechanisms of cytotoxic T-lymphocyte (CTL) and NK cells. Expression of a pro-Smac fusion protein by D5 tumor cells greatly enhanced the susceptibility to killing by lymphokine-activated killer (LAK) cells or purified GrB. GrB-mediated killing was increased to a much greater extent when tumor cells expressed the eGFP-Smac fusion protein with a GrB cleavage site compared to a caspase 8 cleavage site. In contrast, perforin-deficient LAK cells, which lack GrB-mediated cytotoxicity but process normal ligands for death receptors, killed D5 tumor cells expressed pro-Smac with caspase 8 cleavage site more efficiently. Enhanced killing by GrB was also accompanied by processing of the fusion protein and increased caspase-3-like activity. These results indicate that killing of tumor cells can be amplified by targeting cell-mediated cytotoxic mechanisms via expression of pro-Smac fusion proteins.

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